

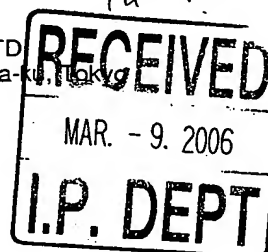
From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44bis.3(c) and 72.2)

To:

KYOWA HAKKO KOGYO CO. LTD.
6-1, Ohtemachi 1-chome, Chiyoda-Ku, Tokyo
1008185
JAPON



Date of mailing (day/month/year)

02 March 2006 (02.03.2006)

Applicant's or agent's file reference
1548**IMPORTANT NOTIFICATION**International application No.
PCT/JP2004/004611International filing date (day/month/year)
31 March 2004 (31.03.2004)

Applicant

KYOWA HAKKO KOGYO CO. LTD. et al

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Yoshiko Kuwahara

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 1548	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2004/004611	International filing date (<i>day/month/year</i>) 31 March 2004 (31.03.2004)	Priority date (<i>day/month/year</i>) 31 March 2003 (31.03.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant KYOWA HAKKO KOGYO CO. LTD.		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	This REPORT consists of a total of 6 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 80%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input checked="" type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VII	Certain defects in the international application																							
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 740 14 35</p>	<p>Date of issuance of this report 22 February 2006 (22.02.2006)</p> <p>Authorized officer Yoshiko Kuwahara</p> <p>Telephone No. +41 22 338 90 90</p>
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PATENT COOPERATION TREATY

Translation

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

<div style="border: 1px solid black; width: 100%; height: 100%;"></div>		Date of mailing (day/month/year)
Applicant's or agent's file reference 1548		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/JP2004/004611	International filing date (day/month/year) 31.03.2004	Priority date (day/month/year) 31.03.2003
International Patent Classification (IPC) or both national classification and IPC		
Applicant KYOWA HAKKO KOGYO CO. LTD.		

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/004611

Box No. I

Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language
_____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/004611

Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 4-6

because:

☒ the said international application, or the said claims Nos. 4-6
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The inventions of claims 4-6 concern treating the human body by therapy (PCT Article 34 (4)(a)(i) and PCT Rule 67.1(iv).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 4-6

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/004611

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-3, 7-9	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-3, 7-9	NO
Industrial applicability (IA)	Claims	1-3, 7-9	YES
	Claims		NO

2. Citations and explanations:

The opinion in this report is based on the following documents cited in the international search report.

- Document 1: WO 96/36624 A1 (Kyowa Hakko Kogyo Co., Ltd.) & EP 771794 A1
- Document 2: WO 03/016279 A1 (Tanabe Seiyaku Co., Ltd.) & EP 1424326 A1
- Document 3: WO 02/098880 A1 (BAYER AKTIENGESELLSCHAFT)
- Document 4: JP 2002-537383 A (Merck Frosst Canada & Co.) & EP 1157007 A1
- Document 5: WO 00/51598 A1 (SMITHKLINE BEECHAM CORPORATION)
- Document 6: Masayoshi ISHIBASHI et al., Gendai Iryo, 2002, 34(9), pp. 2249-2254
- Document 7: Naomi YAMASHITA, Biomedicine & Therapeutics, 2001, 35(11), pp. 1225-1226
- Document 8: Yukio NAGASAKA, Kokyu to Junkan, 1996, 44(8), pp. 839-845
- Document 9: HAEFNER, D., et al., Am. J. Respir. Crit. Care Med., 2000 161, pp. 1495-1500
- Document 10: TEIXEIRA, M.M., et al., TIPS, 1997, (18), pp. 164-170

○Claims 1-3 and 7-9

Document 1 (Example 140) describes a compound that has PDE4 inhibitory activity and has the structure represented by Formula (I) of this application, and the specification (page 1, line 4 to page 3, line 23) describes the use of that compound as a medicine. This being the case, when we compare the inventions of claims 1-3 and 7-9 with the invention described in document 1, the former differs from the latter because its application is the treatment of pulmonary diseases associated with neutrophilic inflammation, and more specifically, COPD, ARDS, etc.

However, it is publicly known from documents 2-9 that ingredients that have PDE4 inhibitory activity are useful in the treatment of COPD and lung tumors, and from documents 2-4, 9, and 10 that such ingredients are useful in the treatment of ARDS and acute lung trauma. Moreover, as described in documents 3 and 5-8, it is publicly known that these diseases are associated with neutrophilic inflammation. Thus, this examination finds that persons skilled in the art would require no particular ingenuity to use the compound that has PDE4 inhibitory activity and has the structure represented by Formula (I) of this application described in document 1 for the prevention and treatment of COPD, ARDS, etc.

As a result, based on the descriptions in documents 1-10, the inventions of claims 1-3 and 7-9 lack an inventive step.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/004611

Box No. VI Certain documents cited

1. Certain published documents (Rule 43bis.1 and 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/066044 A1 [EY]	14.08.2003	31.01.2003	08.02.2002
WO 2004/005276 A1 [EY]	15.01.2004	03.07.2003	03.07.2002
WO 03/080049 A1 [EY]	02.10.2003	20.03.2003	20.03.2002 07.01.2003

2. Non-written disclosures (Rule 43bis.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
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